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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 11/12/2004

11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/934,025	BECKMANN ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-40 and 43-46* is/are pending in the application.

4a) Of the above claim(s) *,19,20 and 31-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-30 and 43-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *08/21/01, 2 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group III (claims 21-30 and 43-46) in the reply filed in Paper number 5 submitted October 30, 2003 is acknowledged. The traversal is on the ground(s) that "...examination of the claims in Groups II-V would not create an undue burden...". This is not found persuasive because the Groups are classified differently and consequently necessitate different searches in the U.S. Patent shoes. The method groups of Inventions III, IV and V utilize different reagents, involve different method steps and yield different endpoints, which would require additional searching. This reasoning is noted in the election/restriction requirement mailed September 26, 2003 as Paper number 3. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Clearly different searches and issues are involved in the examination of each group.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 19-40 and 43-46 are pending.

Claims 1-18, 41 and 42 have been cancelled.

Claims 43-46 have been added.

Claims 19, 20 and 31-40, drawn to non-elected inventions are withdrawn from examination.

Claims 21-30 and 43-46 are examined on the merits.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 27 is rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials.

The specification lacks complete deposit information for the deposit of hybridoma cell lines 1F6D8, 1B2C11, 3A1C11, 2C1H7, 3F2A4, 5FC11, 6D4D11, 3D12D1, 4B6G6, 5F1D4, 6H8E3, 6H10C7, 3E10A3, 6A7F9 and 6E7G1. It is not clear that the cell lines possessing the identical properties of these hybridoma cell lines are known and publicly available or can be reproducibly isolated from nature without undue experimentation.

Exact replication of a cell line is an unpredictable event. Although applicant has provided a table, Figure 2B summarizing properties of the designated monoclonal antibodies and a method for producing antibodies that react specifically with modified β-tubulin, the process of selecting the claimed hybridoma cell lines and monoclonal antibodies will not necessarily reproduce antibodies and hybridomas which are chemically and structurally identical to those claimed. It is unclear that one of skill in the

art could derive antibodies and hybridomas identical to those claimed. Undue experimentation would be required to screen all of the possible antibody and hybridoma species to obtain the claimed antibodies and hybridomas.

Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed hybridoma cell lines, a suitable deposit of hybridoma cell lines 1F6D8, 1B2C11, 3A1C11, 2C1H7, 3F2A4, 5FC11, 6D4D11, 3D12D1, 4B6G6, 5F1D4, 6H8E3, 6H10C7, 3E10A3, 6A7F9 and 6E7G1 patent purposes, evidence of public availability of the claimed cell lines or evidence of the reproducibility without undue experimentation of the claimed cell lines, is required.

If the deposits are made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 22 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitation "the dose of the β-tubulin" in claim 22 lacks proper antecedent bases in independent claim 21.

b. Claim 22 is vague and indefinite in the method step, "further comprising the step of adjusting the dose of the β-tubulin modifying agent administered to the patient". This step is not consistent with the method endpoint of monitoring the amount of modified β-tubulin isotype in a patient, hence the method steps do not correlate with the preamble. Moreover, the optimization of the administration step recited in claim 22 suggests that administration was established in independent claim 21, which it has not. Applicants are requested to clearly set forth a method that is commensurate with the endpoint. And while all of the technical details of a method need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is practiced.

c. The recitations "1F6D8, 1B2C11, 3A1C11, 2C1H7, 3F2A4, 5FC11 and 6D4D11", "3D12D1, 4B6G6, 5F1D4, 6H8E3 and 6H10C7" and "3E10A3, 6A7F9 and 6E7G1" in claim 27 is vague and indefinite. These recitations are laboratory

designations whose identities are not art known. Applicant is advised to amend the claims to include American Type Culture Collection numbers.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 21-30 and 43-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shan et al. (Proc. Natl. Acad. Sci. USA 96: 5686-5691, May 1999/ IDS reference AE, submitted August 21, 2001), and further in view of WO 98/05315 (February 12, 1998/ IDS reference AC, submitted August 21, 2001), U.S. Patent number 4,517,288 (issued May 14, 1985) and Harlow and Lane (Antibodies, A Laboratory Manual, pages 319, 321-325 and 340-352, 1988).

Shan teaches a method of monitoring the amount of modified B-tublin isotype in a sample treated with 2-fluoro-1-methoxy-4-pentafluorophyenylsulfonamidobenzene (T1380670), a synthetic compound that modifies Cys-239 of β_2 and β_4 tubulin isotypes with anti-β tubulin antibodies, see abstract on first page; page 5687, Figure 1; page 5688, column 2, "T138067 Modifies..." section and " T138067 Binds..." section. It is reasonable to conclude that the antibodies of Shan are the same as the β tubulin antibodies in the methodology claimed in light of the fact they possess the same binding

affinity to Cys-239 of β_2 and β_4 tubulin isotypes. Shan does not teach that the sample is from a patient, a standard curve is conducted and an adjusted dose of the anti-β tubulin modifying agent is administered to the patient. Shan also does not teach that the antibody is covalently linked to a detectable moiety.

However, WO 98/05315 teaches pentafluorobenzensulfonamides and analogs within pharmaceutically acceptable compositions administered to patients in varying dosages ranging from about 2 mg up to about 2,000 mg per day with variations dependent upon the disease target, the patient and the route of administration, see page 28, line 20-page 29, line 2. And U.S. patent #4,517,288 teaches the implementation of biological assays wherein patient serum may be tested on a solid matrix. The patent also sets forth establishing a calibration curve, column 1, lines 49-66; column 2, lines 31-33. Moreover, Harlow and Lane teach the labeling of antibodies to be used in a wide range of immunological techniques, see pages 217, 321-324, 340, 342, 343 and 353. The antibodies can be labeled with an enzyme, biotin, fluorochromes and iodine as listed on page 322.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention to establish a method of monitoring the amount of β–tubulin isotype in a patient treated with T1380670 because pentafluorobenzensulfonamide compositions have demonstrated pharmacological activity in *in vitro* and *in vivo* assays, see WO document, page 27, line 6-page 28, line 18 and it is clear that T1380670 had antitumor efficacy in mouse xerograph models, see

page Shan, page 5691, "T138067 Is Efficacious...."section and. One of ordinary skill in the art would have been motivated to combine all of the listed teachings in order to determine efficacy of specific doses of T138067 and thereby establish its clinical usefulness in the human treatment of multidrug-resistant (MDR) tumors, see abstract of Shan.

It also would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to utilize the teachings of U.S. Patent #4,517,288 and Harlow and Lane. The patent states that protocols implementing ligand assays and immunochemical assays have wide variety utilities including correlating known concentrations of a test sample versus an unknown concentration and testing analytes within patient serum, blood or urine, see column 1, lines 49-66; column 3, lines 20-45 and column 4, lines 41-58. Harlow and Lane's basic antibodies manual provides protocols standardly used in immunology techniques. One of ordinary skill in the art would have been motivated to implement the teachings of all the references in order to create β–tubulin antibody-conjugates and monitor the amount of β–tubulin modifying agent in a patient sample in order to use them in a number of applications such as quantitative assays, pharmacokinetic assays, as well as for the discovery of new approaches to antitumor therapy. Furthermore, it is clear that T138067 displayed cytotoxic effects against MDR human tumor cells in culture and in mouse xenograft models one of ordinary skill in the art would have been motivated to monitor the amount of β–tubulin modifying agent in a patient sample to ascertain information on the

effectiveness of the pentafluorobenzensulfonamide composition in humans using the antibody reagents, see Shan, page 5686, column 2, first full paragraph.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The examiner works a flexible schedule, but can normally be reached between the hours of 6:30 am to 5:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
29 October 2004